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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,258	10/07/2003	Francesco Orlandi	51637/76	3122

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EXAMINER	
CLOW, LORI A	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 03/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/679,258	ORLANDI ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *5/16/05;10/7/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *0206* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicants' response, filed 12 December 2005, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-38 are currently pending.

Drawings

The replacement drawing for Figure 1, submitted 16 May 2005 is accepted. The drawings submitted 7 October 2003 (Figures 2 and 3) are also accepted.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,573,103 B1(Wald), further in view of Stempfle et al. (Pediatric Radiology (1999) Vol. 29, pages 682-688), for the reasons set forth in the previous Office Action and re-iterated below.

The instant claims are drawn to a method of assessing a patient's risk of having a fetus with fetal abnormality comprising determining BPD/OFD ratio, determining a secondary marker, performing a comparison of the BPD/OFD ratio and the secondary marker to relative frequency distributions obtained from known affected and unaffected pregnancies, thereby assessing a patient's risk of having a fetus with a fetal abnormality.

In regard to claims 1-5 and 7-38, Wald teaches a method for screening for fetal Down's syndrome in which marker levels are measured in order to calculate risk of Down's syndrome(chromosomal abnormality/trisomy 21) (abstract). In particular, Wald teaches assaying a sample obtained from a pregnant woman at a first stage of pregnancy from at least one biochemical screening marker and/or from at least one ultrasound screening marker, assaying a sample obtained from a pregnant woman at a second stage of pregnancy from at least one biochemical screening marker and/or from at least one ultrasound screening marker, and determining the risk of Down's syndrome using the markers levels. The risk may be determined by a statistical analysis based upon reference data derived from existing or future studies (column 2, lines 5-32). Wald also teaches that this method may be used with AFP in screening for open neural tube defects (spina bifida) (column 2, lines 66-67 to column 3, lines 3) (1-5, 29 and 30).

The biochemical markers can include AFP, hCG, PAPP-A, and others listed at column 4, lines 51-67. The ultrasound markers can include nuchal translucency thickness, nuchal fold thickness, femur length and others listed at column 5, lines 1-12 (7-11).

Wald teaches that the single risk estimate in the invention is derived from measurements of marker levels carried out on biochemical samples and/or utlrasound images which are obtained sequentially at two or more different stages of pregnancy. The calculation can be integrated as a single test at one stage (column 5, lines 26-31).

Calculation of risk from the measured marker levels is based upon the relative frequency distribution of marker level in Down's syndrome (affected) and unaffected pregnancies. Any of

the known statistical techniques may be used, but the multivariate Gaussian model is preferred (column 6, lines 19-column 9) (claims 12-16).

Standard deviations, correlation coefficients, and means (MoM) for unaffected and Down's syndrome pregnancies for screening markers (based on the gestational age estimate using ultrasound scan examination, with maternal weight adjustment of serum markers (normalization) is depicted in Table 1 (claims 17-18).

The multivariate Gaussian analysis of the MoM for all markers from each stage of pregnancy is performed to give distribution parameters, which may then be used for assessing overall risk or age-specific risk (column 13, lines 14-43) (claims 19-27).

Screen positive and screen negative evaluations can be determined from the various implemented steps described above based upon evaluation cut-off values (column 13) (claim 28).

Finally, Wald teaches that this process can be automated (abstract and column 3, lines 33-43) (claim 30).

Wald does not specifically teach using the ultrasound marker BPD/OFD in the evaluation of patient risk for having a fetus that is abnormal (step 1 of claim 1 and dependent claims, claims 28-30). However, Stempfle et al. do teach that biometrical and morphological criteria have been used in fetal screening of Down's syndrome. More specifically the bi-parietal diameter/occipto-frontal diameter ratio (BPD/OFD) has been employed in numerous studies as an indication of trisomy 21 (see abstract and see page 686, column 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time of invention to use the ultrasound marker of BPD/OFD ratio of Stempfle et al. in the methods taught by Wald, as the primary marker. Wald motivates one to utilize such a marker at column

5, line 5, where he lists a series of ultrasound imaging markers and states that "measurements carried out on ultrasound images may include one or more of the following ultrasound markers of Down's syndrome, among others", thus also providing one with a reasonable expectation of success in using any known ultrasound marker.

Response to Applicant's Arguments with regard to Wald in view of Stempfle

Applicant argues that "the very point of Wald is to take markers from a first and second stage of pregnancy (see abstract). Therefore, even if Stempfle teaches that one marker can be a determination of the cephalic index, Wald expressly teaches away from using such a measurement of the cephalic index taken during the first trimester with another marker also taken at the first trimester, as recited in the present claims".

This is not persuasive because Wald does teach taking measurements assaying a sample obtained from a pregnant woman at a first stage of pregnancy for at least one biochemical marker and measuring at least one screening marker from an ultrasound scan taken at a first stage of pregnancy (column 3, lines 10-14). Wald does not teach away from measuring both at the first trimester of pregnancy, as suggested by Applicant. Wald, in fact, claims a method by which samples for biochemical screening are taken at the first trimester of pregnancy and ultrasound measurements are taken at the first trimester of pregnancy. If the woman is classified as screening negative, then second semester tests are performed. However, if not, the first trimester tests are used to determine Down syndrome risk (see column 16, claim 20).

Therefore, Wald in view of Stempfle still make obvious the instantly claimed invention. No claims are allowed.

Conclusion

The outstanding rejection under 35 USC 112, 1st paragraph for New Matter has been withdrawn in view of Applicants amendments to the claims and in view of the interview conducted 19 December 2005.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

February 28, 2006
Lori A. Clow, Ph.D.
Art Unit 1631
Lori A Clow
Patent Examiner